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Substi	tute for form 1449A/P	то			Complete if Known			
. 0000-				Application Number	09/883,033			
	PPLEMEN			Filing Date	June 15, 2001			
	FORMATIO		2.1 (19.8)	First Named Inventor	Jean-Pierre Sommadossi et al.			
ST	ATEMENT	BY APPI	LICANT	Group Art Unit	1623			
(use as many sheets as necessary)				Examiner Name	Howard V. Owens, Jr.			
Sheet	1	of	9	Attorney Docket Number	06171.105026 (IDX 1005 US)			

5. 1			U.	S. PATENT DOCUMENTS			
Examiner Cite No. 1		U.S. Patent Do Number	Kind Code (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages/Relevant Figures Appear	
		4,916,122		Chu	04-10-1990		
		4,957,924		Beauchamp	09-18-1990		
		5,149,794		Yatvin et al	09-22-1992		
		5,190,926		Chu	03-02-1993	S	
		5,194,654		Hostetler et al.	03-16-1993	0	
		5,223,263		Hostetler et al.	06-29-1993	CT '-n	
-		5,256,641		Yatvin et al	10-01-2693	(A)	
		5,411,947		Hostetler et al.	05-02-1995	:. <u>1</u>	
		5,463,092		Hostetler et al.	10-31-1995	-: :	
		5,539,116		Liotta	07-23-1996	က္	
		5,543,389		Yatvin et al	08-06-1996	0	
		5,543,390		Yatvin et al	08-06-1996	,	
		5,543,391		Yatvin et al	08-06-1996		
		5,554,728		Basava et al.	09-10-1996		
		5,559,101		Weis et al.	09-24-1996		
		5,565,438	1 . 1	Chu	10-15-1996		
		5,567,688		Chu	10-22-1996		
		5,587,362		Chu	12-24-1996		
		5,939,402		Weis et al.	08-17-1999		
		6,025,335	1. 1	Weis et al.	02-15-2000		
		6,194,391		Schinazi et al.	02-27-2001		
		6,245,749		Schinazi et al.	06-12-2001		
-		6,297,222	B1	von Borstel et al.	10-02-2001		

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SUPPLEME			Filing Date	June 15, 2001	
	INFORMATION DISCLOSURE			Jean-Pierre Sommadossi et al.	
STATEMEN	T BY APPI	LICANT	Group Art Unit	1623	
(use as many sheets as necessary)			Examiner Name	Howard V. Owens, Jr.	
Sheet 2	of	9	Attorney Docket Number	06171.105026 (IDX 1005 US)	

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		wo	89/02733		University of California	04-06-1989		L
31		wo	89/03838	Al	Pro-neuron, Inc.	05-05-1989		
		wo	90/00555		Vical, Inc.	01-25-1990		
		wo	91/16920		Vical, Inc.	11-14-1991		
		wo	91/18914		Vical, Inc.	12-12-1991		
		wo	91/19721		Glazier	12-26-1991		L
		wo	92/01138		Yatvin	01-20-1994		
		wo	92/08727					
		wo	92/15308		Wellcome	09-17-1992		L
		wo	92/18517		Yale et al.	10-29-1992		_
		wo	93/00910		Vical, Inc.	01-21-1993		
		wo	94/20523		Burroughs Wellcome	09-15-1994		L_
		wo	94/26273		Hostetler	11-24-1994		
		wo	94/29331		Sloan-Kettering Inst. for Cancer Research	12-22-1994		
		wo	95/07086					
		wo	96/11204		Matthes & Von Jenta-Lipinski	04-18-1996		
		wo	96/13512		Genencor	05-09-1996		
		wo	96/15132		University of California	05-23-1996		
		wo	96/40164		Emory University	12-19-1996		
		wo	98/15563		Pankiewicz, K.W. et al	10-09-1997		_
		EP	0 355 131	Bl	Pro-neuron, Inc.	09-04-1996		
		EP	0 352 248		Medivir Aktiebolag	01-24-1990		
		EP.	0 350 287		Vical, Inc.	02-10-1990		

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Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number. Complete if Known Substitute for form 1449A/PTO Application Number 09/883.033 SUPPLEMENTAL June 15, 2001 Filing Date INFORMATION DISCLOSURE First Named Inventor Jean-Pierre Sommadossi et al. STATEMENT BY APPLICANT Group Art Unit **Examiner Name** Howard V. Owens, Jr. (use as many sheets as necessary)

Attorney Docket Number

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Examiner Initials *	Cite No. 1	For	reign Patent Document  Number Kind Code <sup>2</sup> -  (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document DD-MM-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	7
		EP	0 494 119	BioChem Pharma	07-08-1992		$\perp$
		JР	06-293645	Saneyoshi et al.	10-21-1994		

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		OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
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		ARNER and ERIKSSON, "Mammalian Deoxyribonucleoside Kinases," Pharm. Ther., 1995, 67(2), 155-186.					
		BERK et al., "A Genetically Distinct Tymidine Kinase in Mammalian Mitochondria," J Biol Chem, 1973, 248, 2722-2729.	_				
	BESTWICK et al., "Selective Expansion of Mitochondrial Nucleoside Triphosphate Pools in Antimetabolite-treated HeLa Cells," J Biol Chem, 1982, 257, 9300-9304.						
	BLOCH, et al. "The Role Of The 5'-Hydroxyl Group Of Adenosine In Determining Substrate Specificity For Adenosine Dearminase." J. Med. Chem. 10(5), 908-12 (September 1967).						
		BRIDGES et al., "Characterization of a dCTP Transport Activity Reconstituted from Human Mitochondria," J. Biol. Chem, February 19, 1999, 274(8), 4620-4625.					
		BRIDGES et al., "Identification of a novel mitochondrial dNTP carrier and its interaction with anti-HIV nucleoside analogs," Proc. Am. Assoc. Cancer Res., March 1997, 38, 414.					
		BRIDGES et al., "Inhibition of Mammalian DNA Polymerase-Associated 3' to 5' Exonuclease Activity by 5'-Monophosphates of 3'-Azido-3'-Deoxythymine and 3'-Amino-3'-Deoxythymidine," <u>Biochemical Pharmacology</u> , 1993, 45(8), 1571-1576.					
		BRYANT et al., "Antiviral L-Nucleosides Specific for Hepatitis B Virus Infection," Antimicrobial Agents and Chemotherapy, 45(1), 229-235 (January 2001).					
		CHANG et al., "Biochemical Pharmacology of (+)- and (-)-2',3'-Dideoxy-3'-thiacytidine as Anti-hepatitis B Virus Agents," J Biol Chem, November 5, 1992, 267(31), 22414-22420.					

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	PPLEMENTAI			Filing Date	June 15, 2001	
	FORMATION I			First Named Inventor	Jean-Pierre Sommadossi et al.	
ST	ATEMENT BY	APPL	ICANT	Group Art Unit	1623	
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Sheet	4	of	9	Attorney Docket Number	06171.105026 (IDX 1005 US)	

	٠.	OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS	
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		CHANG, et al., "Deoxycytidine Deaminase-resistant Stereoisomer is the Active Form of (-)-2',3'-thiacytidine in the Inhibition of Hepatitis B Virus Replication," <i>Journal of Biological Chemistry</i> , Volume 267(20), 13938-13942 (July 15, 1992).	
		CHARIOT et al., "Zidovudine-induced mitochondrial disorder with massive liver steatosis myopathy, lactic acidosis, and mitochondrial DNA depletion," J. Hepatology, 1999, 30, 156-160.	
		CHEN et al., "Characterization of Pyrimidine Deoxyribonucleoside Kinase (Thymidine Kinase) and Thymidylate Kinase as a Multifunctional Enzyme in Cells Transformed by Herpes Simplex Virus Type 1 and in Cells Infected with Mutant Strains of Herpes Simplex Virus," <u>J Virol</u> , June 1979, 30, 942-945.	
·		CHEN et al., "Delayed Cytotoxicity and Selective Loss of Mitochondrial DNA in Cells Treated with the Anti-human Immunodeficiency Virus Compound 2',3'-Dideoxycytidine," J Biol Chem, 1989, 264, 11934-11937.	
		CHEN et al., "The Role of Cytoplasmic Deoxycytidine Kinase in the Mitochondrial Effects of the Antihuman Immunodeficiency Virus Compound 2',3'-Dideoxycytine," J Biol Chem, February 15, 1992, 267(5), 2856-2859.	
		CUI et al., "Effect of Nucleoside Analogs on Neurite Regeneration and Mitochondrial DNA Synthesis in PC-12 Cells," J. of Pharmacology and Experimental Therapeutics, 1997, 280(3), 1228-1234.	
		DAVIS et al., "In Situ Localization of Mitochondrial DNA Replication in Intact Mammalian Cells," <u>J Cell Biol</u> , 1996, 135, 883-893.	
		DAVISSON, et al., "Synthesis of Nucleotide 5'-Diphosphates from 5'-O-Tosyl Nucleosides," J. Org. Chem., 52(9), 1794-1801 (1987)	
		DOONG et al., "Inhibition of the replication of hepatitis B virus in vitro by 2',3'-dideoxy-3'-thiacytidine and related analogues," Proc. Natl. Acad. Sci., October 1991, 88, 8495-8499.	
		DU et al, Synthesis, "Anti-Human Immunodeficiency Virus and Anti-Hepatitis B Virus Activities of Novel Oxaselenolane Nucleosides," J. of Med. Chem., (40)19, 2991-2993 (September 12, 1997).	

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-		DUTSCHMAN et al., "Metabolism of 2',3'-dideoxy-2',3'-didehydro-β-L-(-)-5-Fluorocytidine and Its Activity in Combination with Climically Approved Anti-Humna Immunodeficiency Virus β-D-(+) Nucleoside Analogs In Vitro," Antimicrobial Agents and Chemotherapy, July 1998, 42(7), 1799-1804.	
		FURMAN, et al., "The Anti-Hepatitis B Virus Activities, Cytotoxicities, and Anabolic Profiles of the (-) and (+) Enantiomers of cis-5-Fluoro-1-[2-(Hydroxymethyl)-1,3-oxathiolane-5-yl]-Cytosine" Antimicrobial Agents and Chemotherapy, 36(12) 2686-2692 (December 1992).	
	,	GLONEK, et al. "Full anhydrization of methylenediphosphonic acid and of phosphoric acids by a carbodiimide" Inorg. Chem., 1975 Vol. 14 (7); 1597-602.	
		GOSSELIN, G. et al. "Synthesis and Antiviral Evaluation of β-L-Xylofuranosyl Nucleosides of the Five Naturally Occurring Nucleic Acid Bases", <i>Journal of Heterocyclic Chemistry</i> , 1993, 30 (OctNov.), 1229-1233.	
		HERNANDEZ-SANTIAGO et al., "Pharmacology of β-L-Thymidine and β-L-2'-Deoxycytidine in HepG2 Cell and Primary Human Hepatocytes: Relevance to Chemotherapeutic Efficacy against Hepatitis B Virus," Antimicrobial Agents and Chemotherapy, June 2002, 46(6), 1728-1733.	
		HOARD, et al., "Conversion of Mono- and Oligodeoxyribonucleotides to 5'-Triphosphates," J. Am. Chem. Soc., 87(8), 1785-1788 (1965).	
		HOLY. "Nucleic Acid Components and Their Analogs. CLIII. Preparation of 2'-deoxy-L-Ribonucleosides of the Pyrimidine Series," Collect. Czech. Chem. Commun. (1972), 37(12), 4072-87.	
		HOSTETLER, K.Y., et al. "Greatly Enhanced Inhibition Of Human Immunodeficiency Virus Type 1 Replication In CEM And HT4-6C Cells By 3'-Deoxythymidine Diphosphate Dimyristoylglycerol, A Lipid Prodrug Of 3'-Deoxythymidine." (September 1992) Antimicrob Agents Chemother. 36:2025-2029.	
		HOSTETLER, K.Y., et al. "Synthesis And Antiretroviral Activity Of Phospholipid Analogs Of Azidothymidine And Other Antiviral Nucleosides." (April 15, 1990) J. Biol Chem. 265(11):6112-7.	
		IMAI et al., "Studies on Phosphorylation. IV. Selective Phosphorylation of the Primary Hydroxyl Group in Nucleosides." J. Org. Chem., 34(6), 1547-1550 (June 1969).	
		JONES, R. et al., "Mini Review: Nucleotide prodrugs," Antiviral Research, 27, 1-17 (1995).	

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		JUROVČIK and HOLY "Metabolism of pyrimdine L-nucleosides," <u>Nucleic Acids Research</u> , August 1976, 3(8), 2143-2153.	
		KORBA et al., "A cell culture assay for compounds which inhibit hepatitis B virus replication," Antiviral Res., 15:217 (1991).	
		KRAYEVSKY and CHERNOV, "Can a Substrate Enantiomer Be a Substrate for the Same Enzyme?,"  Molecular Biology, 1996, 30(5), 585-591.	
		KRAYEVSKY and CHERNOV, "Should the Asymmetric of Enzymatic Active Centers Always Correlate with the Asymmetry of their Substrates?," J. of Bionolecular Structure & Dynamics, 1996, 14(2), 225-230.	
		KUCERA, L.S., et al "Novel membrane-interactive ether lipid analogs that inhibit infectious HIV-1 production and induce defective virus formation." AIDS Res Hum Retroviruses. 6:491-501 (May 1990).	
		LABENZ et al., "Analysis of the TK Enzyme Complex Induced by HSV Types 1 and 2 by Means of Isoelectric Focusing and Polyacyrlamide Gel Electrophoresis," <u>Arch Virol</u> , 1982, 71, 235-249.	
		LIN et al., "Design and Synthesis of 2',3'-Dideoxy-2', 3'-didyhydro-β-L-cytidine (β-L-Fd4C), Two Exceptionally Potent Inhibitors of Human HBV and Potent Inhibitors of HIV In Vitro," J. Med. Chem., 39(9), 1757-1759 (April 26,1996).	
		LIN et al., "Synthesis and Biological Evaluation of 2',3'-Dideoxy-L-pyrimidine Nucleosides as Potential Antiviral Agents agains HIV and HBV," J. Med. Chem. 1994, 97, 798-803.	
		LIN et al., "Synthesis of Several Pyrimidine L-Nucleoside Analogues as Potential Antiviral Agents,"  Tetrahedron Letters, Vol. 51(4), 1055,1068 (1995).	
		MAGA et al., "Lack of stereospecificity of suid pseudorabies virus thymidine kinase," Biochem. J., 294(2), 381-385 (September 1, 1993).	
		MANSOUR et al., "Stereochemical Aspects of the Anti-HCMV Activity of Cytidine Nucleoside Analogues," Antiviral Chemistry & Chemotherapy, 6(3), 138-142 (1995).	
	<b></b> -	Morris S. Zedeck et al. Pseudomonas testosteroni, Mol. Phys. (1967), 3(4), 386-95.	<u>L</u>
		NAKAYAMA, C., et al., "Synthetic Nucleosides and Nucleotides. XX. Synthesis of Various 1-β- Xylofuranosyl-5-Alkyluracils and Related Nucleosides." Nucleosides, Nucleotides, 1, 139-146 (1982)	

Examiner Signature	Date Considered	

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		NORBECK, Tetrahedron Letters, 30 (46), 6246 (1989)	
		PANKIEWICZ. et al. "Efficient synthesis of methylenebis(phosphonate) analogues of P1,P2-disubtituted phyrophospates of biological interest. (1997-04-15), 119, 3691-3692.	
		PANKIEWICZ. et al. "Synthesis of methylenebis(phosphonate) analogs of ADP Ribose" Collect. Czech. Chem. Commun. (1996-09-23), 61; S92-S-95.	
		PAN-ZHOU et al., "Differential Effects of Antiretroviral Nucleoside Analogs on Mitochondrial Function in HepG2 Cells," Antimicrobial Agents and Chemotherapy, March 2000, 44(3), 496-503.	
		PLACIDI et al., "Cellular pharmacology of β-L-thymidine and β-L-2'-deoxycytidine in HepG2 cells and primary rat, monkey and human hepatocytes," 3 <sup>rd</sup> Int. Conf. Ther. Vir. Hepatitis, abstr. A122, 1999 [Antivir. Ther. 4, Suppl. 4].	
		ROBINS, "Selective Deoxygenation and Modification at C2' of Nucleosides," Nucleic Acids Research Symposium Series, Vol. 11, Pages 1-4, Kyoto, Japan, November 24-26, 1982, A.E. Pritchard (ed.), IRL Press, Ltd., Oxford, England, 1982;	×
		ROBINS, M. J. et al. "Purine nucleosides. XXIX. The synthesis of 2'-deoxy-L-adenosine and 2'-deoxy-L-guanosine and their alpha anomers." J. Org. Chem. March 1970, 35, 636-639.	
		ROBINS, M.J., et al., "Nucleic Acid Related Compounds. 42. A General Procedure for the Efficient Deoxygenation of Secondary Alcohols. Regiospecific and Stereoselective Conversion of Ribonucleosides to 2'-Deoxynucleosides." J. Am. Chem. Soc. 105, 4059-4065 (1983).	
		SANEYOSHI, M., et al., "Synthetic Nucleosides and Nucleotides. XIII. Stannic Chloride Catalyzed Ribosylation of Several 6-Substituted Purines." Chem. Pharm. Bull., 27, 2518-2521 (1979).	
-		SCHINAZI, et al., "Selective Inhibition of Human Immunodeficiency Viruses by Racemates and Enantiomers of cis-5-Fluoro-1-[2-(Hydroxymethyl)-1,3-Oxathiolane-5-yl] Cytosine," Antimicrobial Agents and Chemotherapy, 36(11), 2423-2431 (1992).	
		SCHINAZI, et al., 'Effect of Combinations of Acylovir with Vidarabine or its 'Monophosphate on Herpes Simplex Viruses in Cell Culture and in Mice," Antimicrobial Agents and Chemotherapy, 22(3), 499, (1982).	

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				Filing Date	June 15, 2001		
STATEMENT BY APPLICANT				First Named Inventor	Jean-Pierre Sommadossi et al.		
STATEMENT DI APPLICANT				Group Art Unit	1623		
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		SHUTO, S., et al. "A facile one-step synthesis of 5'-phosphatidylnucleosides by an enzymatic two-phase reaction." <i>Tetrahedron Letters.</i> 28. 199-202 (1987).	1
	 	SODERLUND and ARNER, "Mitochondrial versus Cytosololic Activities of Deoxyribonucleoside Salvage Enzymes," Purine and Pyrimidine Metabolism in Man VIII, A.Shota & M. Taylor (ed.), Plenum Press, New York, 1995, 201-204,	
		SPADARI et al., "L-Thymidine is Phosphorylated by Herpes Simplex Type 1 Thymidine Kinase and Inhibits Viral Growth," J. Med. Chem. (1992), 35(22), 4214-4220.	
		TYRSTED et al. "Inhibition of the synthesis of 5-phosphoribosyl-1-pyrophosphate by 3'-deoxy-adenosine and structurally related nucleoside analogs." <i>Biochim. Biophys. Acta.</i> (February 26, 1968), 155(2), 619-22.	
	_	VERRI et al. "Lack of enantiospecificity of human 2'-deoxycytidine kinase: relevance for the activation of beta-L-deoxycytidine analogs as antineoplastic and antiviral agents." <i>Molecular Pharmacology</i> . (January 1997), 51(1), 132-138.	
		VERRI et al., "Relaxed Enantioselectivity of Human Mitochondrial Thymidine Kinase and Chemotherapeutic Uses of L-Nucleoside Analogues," <i>Biochem. J.</i> (1997), 328(1), 317-320 (November 15, 1997).	
		von JANTA-LIPINSKI et al., "Newly Synthesized L-Enantiomers of 3'-Fluoro-Modified $\beta$ -2'-Deoxyribonucleoside 5'-Triphosphates Inhibit Hepatitis B DNA Polymerase but not the Five Cellular DNA Polymerases $\alpha$ , $\beta$ , $\gamma$ , $\delta$ , and $\varepsilon$ Nor HIV-1 Reverse Transcriptase," J. Medicinal Chemistry, 41(12), 2040-2046 (June 4, 1996).	
		Wang, S., Montelaro, R., Schinazi, R.R., Jagerski, B. and Mellors, J.W.: Activity of nucleoside and non-nucleoside reverse transcriptase inhibitors (NNRTI) against equine infectious anemia virus (EIAV). First National Conference on Human Retroviruses and Related Infections, Washington, DC, Dec. 12-16, 1993	. •
		ZEDECK et al. "Pseudomonas testosteroni," <i>Mol. Phys.</i> (1967), 3(4), 386-95.  ZHANG, W., et al. "Removal of Silyl Protecting Groups from Hydroxyl Functions with Ammonium Fluoride in Methanol." <i>Tetrahedron Letter.</i> , 33, 1177-1180 (192).	•

Examiner	• •	Date	
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		ZHU et al., "Anti-Hepatitis B Virus Activity and Metabolism of 2',3'-dideoxy-2',3'-didehydro-β-L-(-)-5-Fluorocytidine," Antimicrobial Agents and Chemotherapy, July 1998, 42(7), 1805-1810.			
		ZHU et al., "Incorporation of Nucleoside Analogs into Nuclear or Mitochondrial DNA Is Determined by the Intracellular Phosphorylation Site," J Biol Chem, 2000, 275(35), 26727-26731.			
		ZHU et al., "Inhibition of Replication of Hepatitis B Virus by Cytallene In Vitro," Antimicrobial Agents and Chemotherapy, August 1997, 41(8), 1755-1760.			

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